dosis should be aggressively corrected in patients at high risk for bilirubin encephalopathy. This is particularly important in patients with respiratory acidosis because carbon dioxide rapidly equilibrates across the blood-brain barrier and increases the cerebral flow and bilirubin delivery to the brain.

For well, term babies without hemolysis or a serum bilirubin level well above 20 mg per dl, there is remarkably little evidence for adverse effects caused by bilirubin on intelligence quotient, neurologic function, or hearing. In fact, the diagnosis of neonatal jaundice as a "problem" may have negative consequences on maternal behavior and attitudes in the early, crucial months of infant development.

Nonetheless, the effects of hyperbilirubinemia in premature infants, who have an increased bilirubin production compared with term infants, and term infants who have increased bilirubin production because they are sick or have hemolytic disease may be deleterious and different from those in well, term infants. Because a degradation of heme results in the equimolar production of carbon monoxide (CO) and bilirubin, the respiratory CO excretion rate, the end-tidal CO concentration, and the blood carboxyhemoglobin level can be used as indices of bilirubin production. Noninvasive technology currently exists for detecting an excessive production of bilirubin even before the development of jaundice.

Currently the two most widely used treatments for exaggerated neonatal hyperbilirubinemia are phototherapy and exchange transfusion, therapies which remove bilirubin that has already been produced. The suppression of bilirubin formation, however, is a more logical preventive strategy, particularly when reserved for those patients who produce an excessive amount of the pigment. The first and rate-limiting step in the degradation of heme to bilirubin is catalyzed by the microsomal enzyme heme oxygenase. Numerous inhibitors of heme oxygenase have been identified, including tin, zinc, chromium, and manganese porphyrin complexes. Zinc protoporphyrin has recently been shown to inhibit bilirubin production and ameliorate hemolytic jaundice in nonhuman rhesus primates.

Two other pharmacologic strategies for ameliorating neonatal jaundice are also being considered. One involves bilirubin oxidase, a mitochrondrial enzyme that is capable of breaking down bilirubin to biliverdin and has been used in rodents with a congenital deficiency of glucuronyl transferase to interrupt the enterohepatic circulation of bilirubin. Another involves a traditional Chinese herbal concoction called *yin zhi huang,* which has been used in Asia to treat hepatitis and neonatal jaundice and has undergone some recent studies showing that it enhances bilirubin clearance from plasma and increases the conjugation of bilirubin by the liver.

Any new strategies to provide more specific therapies for infants at risk for dangerous neonatal jaundice should be combined with screening programs to identify infants who produce excessive amounts of bilirubin and who are at risk for potentially dangerous jaundice. Thus, infants who are at low risk for potentially dangerous neonatal jaundice could be spared an unnecessary use of laboratory testing and therapies.

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Interventional Catheterization for Congenital Cardiac Defects

HEART DEFECTS ARE the most common serious congenital anomalies. Interventional catheterization has had a major effect on the prognosis and costs of these defects. As many as 20% of structural cardiac defects can now be treated effectively in the cardiac catheterization laboratory, and this percentage could approach 40% in the near future. Therapy without thoracotomy, transfusion, or even an overnight stay in a hospital is now possible.

The list of potential uses of balloon valvuloplasty or angioplasty techniques is long and includes valvar and arterial pulmonic stenosis, aortic stenosis, coarctation, rheumatic mitral stenosis, and postoperative stenotic lesions. The greatest success and effect to date has been with valvar pulmonic stenosis. More than 800 balloon pulmonary valvuloplasties have been reported to an international registry. The transvalvar gradient was reduced greater than 70% with a mortality rate of 0.2%. The procedure was less effective in patients with a dysplastic pulmonary valve as is seen in Noonan's syndrome.

Survival rates and gradient reduction for balloon pulmonary valvuloplasty in infants with critical pulmonic stenosis have exceeded those of surgical valvotomy. Cyanotic heart defects with restricted pulmonary blood flow can also be palliated by balloon pulmonary valvotomy, obviating the need and problems associated with a Blalock-Taussig shunt or its variants. Many other stenotic lesions can be dilated, with current results approximating those of surgical outcome, but at lower cost financially and emotionally. The risks of restenosis of dilated arterial segments can be diminished with the use of intravascular stents.

Interventional procedures place great demands on the catheterization team and require experience and coordination. Complications may occur with valvuloplasty, including blood loss, obstruction of femoral vessels, vessel rupture, perforation, and valve destruction with insufficiency. The largest reported complication rate is about 12%, of which half were considered major. The incidence of complications is inversely related to a patient's age. Most complications occur in the very young where the necessity for operator experience and appropriate equipment size is the greatest. In some series, femoral vessel obstruction may occur in as many as 10% of angioplasty-treated children but usually can be treated medically. The overall mortality rate is, however, low (about 0.7%). Because of the potential serious complications, a surgical team should be available to minimize mortality. The economic effects of angioplasty-valvuloplasty procedures can be substantial with most interventional catheterizations costing 20% to 50% of a comparable operative procedure.

Catheter techniques to occlude pathologic or postoperative cardiac or great vessel communications have also become well established. Metallic coils or detachable balloons can be used to permanently occlude systemic-to-pulmonary

artery collaterals, residual aorticopulmonary shunts, persistent left superior venae cavae, and arteriovenous malformations. The current success with patent ductus arteriosus occlusion devices will make their use the treatment of choice for older children with this defect. The demonstrated efficacy of the double umbrella or clamshell occlusion device for atrial septal defect and muscular ventricular septal defect should lead to prompt Food and Drug Administration approval and widespread clinical use. Additional interventional advances are on the horizon and will continue to improve the prospects for a near-normal quality of life for infants born with congenital heart disease. Cost savings will effectively allow for increased access to care within budgetary constraints.

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Diagnosis and Treatment of the Acquired Immunodeficiency Syndrome in Children

THE ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) in children—symptomatic human immunodeficiency virus (HIV)—is becoming one of our nation's largest health problems; 3,213 cases of AIDS in children, ages 0 to 19, have been reported to the Centers for Disease Control (CDC) as of October 1, 1990. They represent about 2% of the total AIDS cases in the United States, now numbering more than 150,000. Further, there is considerable underreporting of pediatric AIDS because rigid criteria are necessary. It is estimated there may be as many as threefold more unreported pediatric AIDS cases in the US. It will soon be the fifth leading cause of death in children. Indeed, about 2,000 infants with HIV infection will be born to about 5,600 HIV-infected mothers annually in the US. Most of the cases are in the urban areas of populous states such as New York, New Jersey, Florida, Texas, and California.

Nearly all HIV-infected children have acquired their disease perinatally from their HIV-infected mothers. Transfusion-acquired cases make up only 11% of the total reported cases, and nearly all of these patients were infected before April 1985, when the routine testing of blood products commenced. Mothers have become infected because of their own intravenous drug use (51%) or their sexual partner's seropositivity (38%), usually also a result of intravenous drug use. Most of these mothers are members of disadvantaged minorities, particularly African American (51%) or Hispanic (20%). (These groups make up 18% of the total US population.) Thus, pediatric AIDS is now a disease of urban disadvantaged minority populations.

Infants and children with HIV characteristically get sick 6 to 18 months after infection; the first manifestation usually is recurrent respiratory tract infection, particularly bacterial or viral pneumonia. *Pneumocystis carinii* infection, candidiasis, persistent diarrhea, and poor growth are also noted early. Encephalopathy occurs in many children as the illness progresses, leading to intellectual and motor deterioration. Some older children get a characteristic pulmonary disorder, lymphoid interstitial pneumonitis, producing diffuse nodular or reticular pulmonary infiltrates and progressive dyspnea. The cause is not known.

A physical examination may reveal prominent lymphadenopathy and hepatosplenomegaly. Parotitis may also be present. Other features such as growth failure are nonspecific. Immunologic abnormalities in HIV-infected infants and children include hypergammaglobulinemia; diminished antibody responses, CD4 cell (T-helper) depletion; reversal of the CD4 to CD8 (T-helper:T-suppressor) ratio; and poor results on functional tests of cellular immunity, such as proliferative responses to mitogens.

Table 1 suggests which infants and children may have HIV infection and should have an HIV-antibody test. A positive HIV-antibody test by screening enzyme-linked immunosorbent assay and confirmatory Western blot test generally indicates HIV infection in children older than 15 months.

Diagnosing HIV disease by antibody testing in infants is complicated by the presence of transplacental maternal HIV antibody in infants' circulation until as old as 15 months. The best way to establish a diagnosis in these infants is to identify HIV by culture of a patient's lymphocytes. The presence of HIV antigen (p24) in the plasma also is diagnostic, but it often is not present in early illness. The polymerase chain reaction to detect viral DNA promises to be a sensitive and specific test, but it is not routinely available.

Treatment is now available that will prolong life and prevent opportunistic infection in children with AIDS. *P carinii* pneumonia prophylaxis with the combination drug trimethoprim and sulfamethoxazole is recommended for all infants younger than 15 months with established HIV infection regardless of immunologic state, any older HIV-positive child with a CD4 lymphocyte count of less than 0.4×10^9 per liter (400 cells per μl), and any HIV-positive child with a previous *P carinii* infection. Trimethoprim-sulfamethoxazole is given as Bactrim or Septra, 150 mg per m^2 a day of the trimethoprim component, in two divided doses three times a week (Monday, Tuesday, and Wednesday).

The use of zidovudine (AZT) is recommended for chil-

TABLE 1.—*Indications for Testing for Human Immunodeficiency Virus (HIV) in Children and Adolescents*

Who could be tested
Children of HIV-infected parents
Children of "high-risk" parents—IV drug users, prostitutes, bisexuals, past residents of countries where HIV is endemic
Children transfused between 1978 and April 1985, before HIV testing
Children transfused after April 1985 in whom clinical or laboratory features of immunodeficiency develop
Children with hemophilia who received clotting factor concentrates between 1978 and January 1985, before heat treatment
Children whose parents request testing
Who should be tested
Children with opportunistic infections suggestive of an immunodeficiency
Children with evidence of T-cell immunodeficiency
Children with recurrent infections and hypergammaglobulinemia (IgG plus IgM plus IgA levels >18 grams per liter [>1,800 mg per dl])
Children with unexplained myopathy, nephritis, hepatitis, or progressive neurologic disease
Children who are bone marrow or organ donors
Children at "high risk" due to IV drug use, prostitution, or sex with high-risk persons

Ig = immunoglobulin, IV = intravenous